Rec'd PCT/PTO 15 APR 2005

PATENT COOPERATION TREATY

REC'D 25 OCT 2004
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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 532232000940	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/33366	International filing date *(day/month/year)* 20 October 2003 (20.10.2003)	Priority date *(day/month/year)* 18 October 2002 (18.10.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/70 and US Cl.: 435/5		
Applicant CYLENE PHARMACEUTICALS		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 17 May 2004 (17.05.2004)	Date of completion of this report 20 September 2004 (20.09.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Tim Brown Telephone No. (571) 272-0773

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-25 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of ______.

☒ the claims:
pages 26-27, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of ______.

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of ______.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of ______.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 11 and 13

because:

☒ the said international application, or the said claim Nos. 13 relate to the following subject matter which does not require international preliminary examination *(specify)*:

Claim 11 does not comply with subject matter provisions of PCT Rule 67 because it is drawn to "information characterizing the structure of an antiviral candidate molecule." PCT Rule 67.1(v) prohibits "mere presentations of information."

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-16	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	4-6	YES
	Claims	1-3, 7-12, 14-16	NO
Industrial Applicability (IA)	Claims	1-12, 14-16	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-3, 7-10 and 14-16 lack an inventive step under PCT Article 33(3) as being obvious over Whitwam (Whitwam "Identification of a Central DNA Flap in Feline Immunodeficiency Virus" Journ. of Virol. (October 2001) Vol. 75, No. 19) in view of Haseltine et al. (US 5,759,768).

Applicants' invention is drawn to a screening assay for identifying molecules for treating HIV, and other retroviral diseases, comprising contacting a candidate molecule with a quadruplex nucleic acid that is at least substantially similar to the central flap nucleic acid sequence of a retrovirus. Applicants' invention provides that the quadruplex is an intermolecular structure, an intermolecular parallel structure, or a dimmer of two intramolecular hairpins. Applicants' invention further provides that the retrovirus at least comprises HIV.

Whitwam discloses a central DNA flap in retroviruses comprising a plus strand of DNA that overlaps the reverse-transcribed retroviral genome (p. 9407, ¶ 1). Whitwam teaches that the central DNA flap is primed by a polypurine tract and that it "plays a role in nuclear import [retroviral] pre-integration complexes" (abstract). Whitwam specifically teaches that the central DNA flap is involved in integration of HIV (p. 9407, ¶ 3)

Whitwam does not expressly teach an assay that screens candidate molecules for interaction with a nucleic acid substantially comprising the central DNA flap. However, Haseltine et al. teach an assay that "can be used to screen for compounds that affect integration of DNA into a target DNA" (column 4, lines 46-48). Haseltine notes that its assay may test the integration of lentiviruses including HIV (column 4, lines 60-63). Because Whitwam discloses that the central DNA flap is critical to retroviral (i.e. HIV) integration, it would have been obvious to include Haseltine et al.'s integration assay in order to identify compounds that affect the activity of the central DNA flap. Thus, Applicants' invention lacks an inventive step over Whitwam. Note that the specific structures for the claimed nucleic acid are inherent to Whitwam's HIV pre-integration complex.

Claims 11 and 12 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Frankel et al. (US 5,654,398).

Whitwam and Haseltine et al. do teach detecting binding of the candidate molecule to the nucleic acid, or circular dichroism. However, Frankel et al. teach a method for identifying HIV therapeutics using circular dichroism to detect interaction between a protein and HIV mRNA comprising a single-stranded non-Watson-Crick base pair sequence (column 1, lines 19-32; column 10, lines 18-26). At the time of Applicants' invention, it would have been obvious to modify Whitwam and Haseltine et al. to include the teachings of Frankel et al as this combination would enable another means for detecting the interaction (i.e. binding) of the candidate compound to the HIV pre-integration complex.

----NEW CITATIONS----

US 5,759,768 (HASELTINE ET AL.) 02 June 1998, column 4, lines 39-63

US 5,654,398 (FRANKEL ET AL.) 06 August 1997, column 10, lines 18-26